UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF OHIO
WESTERN DIVISION

PAMELA RHEINFRANK, INDIVIDUALLY, AND AS PARENT AND NATURAL GUARDIAN OF M.B.D.	:	**Civil Action No. 1:13-cv-144**
	:	**HON. JUDGE SUSAN J. DLOTT**
PLAINTIFFS	:	**PLAINTIFFS' REPLY BRIEF IN FURTHER SUPPORT OF THEIR MOTION TO EXCLUDE IN PART PROFFERED EXPERT OPINIONS OF DR. KWAME ANYANE--YEBOA, DR. ANTHONY SCIALLI, DR. MAX WIZNITZER, AND DR. STEPHANIE GREENE**
V.	:	
ABBOTT LABORATORIES AND ABBVIE INC.	:	**ORAL ARGUMENT REQUESTED**
DEFENDANTS	:	

I. INTRODUCTION

Plaintiffs respectfully request this that Honorable Court exclude in part certain opinions of Defendants' experts, Dr. Kwame Anyane-Yeboa, Dr. Anthony Scialli, Dr. Max Wiznitzer, and Dr. Stephanie Greene, pursuant to Federal Rule of Evidence 702 and *Daubert v. Merrell Dow Pharmaceuticals, Inc*. Defendants' experts are offered to testify that: (1) Plaintiff M.B.D. suffers from Peters-Plus rather than from birth defects caused by Depakote; (2) the Depakote label contained adequate warnings; (3) Plaintiff M.B.D. does not have autism; and (4) Depakote does not cause Chiari I malformation. Because these proffered opinions contravene Rule 702, they must be excluded from evidence.

II. ARGUMENT

A. Motion To Exclude The Testimony Of Dr. Anyane-Yeboa

Abbott offers Dr. Anyane-Yeboa to opine that M.B.D.'s injuries are consistent with

Peters-Plus Syndrome. Plaintiffs move to preclude Dr. Yeboa's opinions concerning Peters-Plus as unreliable.

Plaintiffs' dysmorphology expert, Dr. Howard Saal, has treated M.B.D. since birth. He is the Director of Clinical Genetics at Cincinnati Children's Hospital and has been responsible as her treating dysmorphologist for diagnosing the cause of M.B.D.'s birth defects. The Children's Hospital medical records reflect that Dr. Saal suspected M.B.D.'s birth defects were caused by valproate when he first examined her one day after birth, and that he later confirmed this diagnosis at three months of age. (Saal Dep. 146:19-25, Doc. 125, PageID 14633.) This remains his diagnosis to this date. M.B.D.'s birth anomalies include characteristic facial features of fetal valproate syndrome, developmental delay, Chiari I malformation, Peters Anomaly, and other defects, all of which Dr. Saal attributes to valproate.

Despite Dr. Saal's diagnosis, Defendants offer Dr. Yeboa to opine that M.B.D., whom Dr. Yeboa has never examined, has Peters-Plus Syndrome, an extremely rare genetic condition with a one in one million occurrence rate. (Yeboa Dep. 77:1-10, Doc. 81, PageID 2366.) Dr. Yeboa asserts that Peters-Plus has "never been properly ruled out." However, Dr. Saal is very familiar with Peters-Plus, having published on the syndrome and treated prior patients, and he testified that he considered but rejected Peters-Plus based on M.B.D.'s clinical presentation. He therefore concluded that there was no reason to conduct genetic testing for this particular syndrome because she clearly did not have it.[1] (Saal Dep. 132:19-133:12, Doc.125, PageID14629-30.)

[1] Defendants continue to assert that Plaintiffs' refused genetic testifying. However, no treating doctor has ever recommended this testing, and the Court denied Defendants' belated request for genetic testing; it was not refused by Plaintiffs. (*See* Hearing Transcript Oct. 20, 2014.)

1. Dr. Yeboa Created A Novel Definition Of Peters-Plus Syndrome That Is Unsupported By The Medical Literature

Defendants argue that Dr. Yeboa engaged in a proper differential diagnosis to "rule in" Peters-Plus. However, Dr. Yeboa's methodology is flawed because his definition of Peters-Plus is wholly unsupported by the medical literature. Dr. Yeboa testified that "[e]ssentially, when we say Peters-Plus, you are referring to patients who have Peters anomaly plus something else, okay."[2] (Yeboa Dep. 76:5-7, Doc.81, PageID 2366.) This definition contradicts the entire body of medical literature on Peters-Plus, which is characterized by specific birth defects, including "developmental defects in the anterior chamber of the eye, a typical face, clefting, short limb dwarfism and developmental delay." (Wenniger-Prick, et al, *The Peters' Plus Syndrome: A Review*, Yeboa Dep. Ex. 939, Doc.81-2, PageID 2637.) As noted in Wenniger-Prick, "[m]ost cases have prenatal growth retardation, and virtually all cases are disproportionally short postnatally. Arms and legs are equally shortened…" (*Id.*) As described in this article, 100% of Peters-Plus cases include an eye malformation (98% are anterior chamber defects), as well as short broad hands (brachydactyly.) Further, 98% have Cupid bow upper lip, 95% have short limbs, and 91% clinodactyly of the fifth finger. (*Id.*) Plaintiff M.B.D. lacks many of the features of Peters-Plus such as dwarfism, cardiac malformations, cleft lip and palate, small, malformed ears, short wide hands, fifth finger clinodactyly and Cupid's bow upper lip. (Saal Rebuttal, Dep. Ex. 2, Doc. 124-1, PageID 14526.) Moreover, she has other features, such as microcephaly and Chiari I malformation, that are not considered characteristic of Peters-Plus. In fact, Dr. Yeboa admits he cannot cite to any published articles which report Chiari I associated with Peters-Plus. (Yeboa Dep. 213:13-23, Doc. 81, PageID 2400.)

[2] Contrary to Defendants' assertion, Dr. Saal's testimony does not support Dr. Yeboa's definition of Peters-Plus. Dr. Saal did testify that generally when geneticists look at things, there are reports in the literature of new associations or findings associated with syndromes, exposures or conditions. (Saal Dep. 20:25-22:8, Doc. 124, PageID 14378-80.) However, Dr. Saal was not, as Defendants claim, specifically referring to Peters-Plus.

Defendants attempt to bolster Dr. Yeboa's opinion that Peters-Plus means "patients who have Peters Anomaly plus something else" by citing to published literature; however, no published articles support this proposition. For example, Defendants reference in a footnote Thompson, et al., 1993, *Kivlin Syndrome and Peters'-Plus syndrome: are they the same disorder?* (Def. Ex. 7.) Of note, Dr. Yeboa did not cite to this article in his report, rendering Defendants' reliance upon it inappropriate. *Rimbert v. Eli Lilly & Co.*, No. CIV 06-0874, 2009 U.S. Dist. LEXIS 68851 at *60-62 (D.N.M. July 21, 2009) (articles not referenced by the expert witness cannot be considered in ruling on a *Daubert* motion.)[3] Nonetheless, contrary to Defendants' suggestion, this article does not establish that Peters Anomaly *plus any other defect* constitutes Peters-Plus. Instead, the authors provide a very specific definition of Peters-Plus, which includes: "1) Anterior chamber defects, most commonly Peters' anomaly; 2) short stature with relatively short limbs and brachydactyly. Birth weight is often low; 3) Developmental delay of variable degree; … 4) Characteristic facies with a round face, thin upper lip in a cupid's bow, long philtrum, hypertelorism, short palpebral fissures and early micrognathia. The head is relatively large compared to the height." (Def. Ex. 7, Page ID24764.) (Besides her lack of many of these findings, M.B.D. also has microcephaly, as opposed to a large head.) Similarly, Defendants inappropriately rely upon the earlier article by Cabral de Almeida, et al. (1991) entitled *Short stature, brachydactyly, and Peters' anomaly (Peters'-plus syndrome): confirmation of autosomal recessive inheritance*. Here the author describes two siblings, both of whom have "shortness of the limbs" in addition to short stature, brachydactyly, Peters Anomaly and the characteristic facial features previously described. Neither article supports the claim that Peters Anomaly plus any other random defect constitutes Peters-Plus Syndrome. Instead, these

[3] In accordance with the Court's Standing Order on Civil Procedures, all unreported cases are attached hereto as Ex. A.

articles consistently describe key features, many of which are not displayed by Plaintiff M.B.D. (such as brachydactyl, short limbs, Cupid's bow lip, large head, hypertelorism), as central to the Peters-Plus diagnosis.

There is simply no medical support for the proposition that Peters Anomaly plus any other defect constitutes the genetic syndrome described as Peters-Plus. Dr. Yeboa's attempt to ignore characteristic features of Peters-Plus that M.B.D. simply does not have, such as short limbs (aka dwarfism), brachydactyly (short, stubby hands and fingers), and a Cupid's bow upper lip, renders his opinions unreliable. His definition of Peters-Plus is unsupported by any medical literature and indeed contradicts established diagnostic criteria for this syndrome.

2. Defendants' Dispute Over The One In One Million Occurrence Rate Is Specious

Defendants argue that the relevant incidence rate of Peters-Plus should be the rate of Peters-Plus in those diagnosed with Peters Anomaly instead of the general population. That simply makes no sense. Defendants are arguing that Plaintiff M.B.D. suffers from Peters-Plus. Dr. Yeboa testified that Peters-Plus is a rare genetic condition with a one in 1,000,000 occurrence rate; he did not qualify his answer in any manner. (Yeboa Dep. 77:1-10, Doc. 81, PageID 2366.) Peters Anomaly, on the other hand, is not exclusively a genetic condition, and in fact has been reported with teratogenic exposures, including exposure to antiepileptic drugs. (Yeboa Dep. 94:10-100:12, Doc. 81, PageID 2371-72.) The one in 1,000,000 risk of inheriting a specific genetic syndrome is not affected by the prevalence in which one subcategory of injury in the syndrome occurs from other causes.

3. Dr. Yeboa's Opinion Concerning Genetic Testing Is Unreliable

Dr. Yeboa opines that genetic testing to exclude Peters-Plus must be conducted before diagnosing valproate teratogenicity as the cause of M.B.D.'s birth defects. (Yeboa Report, Dep.

Ex. 927, Doc. 81-1, PageID 2454.) Specifically, he opines that M.B.D. must undergo entire genome sequence testing, and that such testing would reveal she has a genetic abnormality that caused her to suffer "Peters-Plus," as defined by him. However, his opinion concerning genetic testing is unreliable and speculative, because he refuses to concede that a specific gene abnormality, as identified in the medical literature, is the cause of Peters-Plus. Instead, even though the medical literature identifies the B3GALTL gene as the cause of Peters-Plus (Oberstein, et al., Yeboa Dep. Ex. 942, Doc. 81-2, PageID 2659), Dr. Yeboa speculates that some other gene may also be the cause. Therefore, even if Plaintiff underwent genetic testing for the B3GALTL gene and it came back normal, (as it undoubtedly would since she does not have the phenotype for Peters-Plus), Dr. Yeboa would still claim that M.B.D. has Peters-Plus anyway, and that it was caused by some other heretofore unknown, hypothetical gene mutation. (Yeboa Dep. 220:13-18, Doc. 81, PageID 2402.) Obviously, since Dr. Yeboa formed this opinion out of thin air, he cannot identify which gene this would be, nor provide any scientific basis or support for his claim that M.B.D. has any gene mutation. Further, he has no basis to claim that any hypothetical genetic abnormality caused M.B.D. to suffer from Peters Anomaly and all her other birth defects, nor that these injuries constitute Peters-Plus. (Yeboa Dep. 220:1-221:12, Doc. 81, PageID 2402.)

In conclusion, Dr. Yeboa's methodology is flawed as he has no reliable methodology to rule in Peters-Plus. Neither the clinical presentation of M.B.D. nor the statistical odds of Peters-Plus support this diagnosis. His opinion that her injuries are more likely than not caused by a hypothetical gene mutation that cause a new presentation of "Peters-Plus" must be excluded as unreliable.

B. Motion to Exclude the Testimony of Dr. Anthony Scialli

Abbott offers Dr. Scialli to testify about genetics (Peters-Plus), Depakote labeling, and Abbott's regulatory compliance. However, Dr. Scialli lacks the appropriate qualifications and/or basis to opine on these issues and, therefore, his opinions must be excluded.

1. Dr. Scialli Is Not Qualified To Diagnose Peters-Plus

Defendants claim that "Dr. Scialli has not diagnosed M.B.D. with Peters-Plus." In fact, Dr. Scialli's report states: "No one has ruled out Peters-Plus as the cause of [M.B.D.'s] defects, and based on the records it appears to be **the best diagnosis**. . . . [M.B.D.'s] constellation of symptoms is more consistent with **a diagnosis of Peters-Plus** syndrome than with the diagnosis of fetal valproate syndrome/embryopathy reflected in [M.B.D.'s] medical records." (Scialli Report, Dep. Ex. 950, Doc. 129-1, PageID 15249, 15255.) (emphasis added.) Contrary to Defendants' assertion, Dr. Scialli is offering a diagnosis of Peters-Plus.

Dr. Scialli is not qualified to render an opinion that M.B.D. has Peters-Plus. Despite the fact that Dr. Scialli is a practicing OB/GYN and has experience in reproductive and developmental toxicology, he lacks the requisite qualifications to render an opinion as to the cause of M.B.D.'s birth defects; i.e., that M.B.D. has Peters-Plus rather than fetal valproate syndrome. Dr. Scialli does not treat children or diagnose them with common disorders, much less extremely rare genetic disorders like Peters-Plus. (Scialli Dep. 25:2-16, Doc. 129, PageID 15156.) He admits that diagnosing genetic conditions is outside his area of expertise, and he has never been responsible for examining an infant to determine if the child has fetal abnormalities. (Scialli Dep. 24:7-26:10, Doc. 129, PageID 15156.) Dr. Scialli goes beyond the scope of his expertise when he opines that M.B.D. has Peters-Plus and, therefore, his opinions must be excluded. *See, Thomas v. Novartis Pharms. Corp.*, 443 Fed. Appx. 58 (6th Cir. 2011) (court

excluded expert oral surgeons because, although they had experience in treating osteonecrosis of the jaw and read literature on the subject, they were unqualified to determine the cause of plaintiff's osteonecrosis.); *Harvey v. Novartis Pharms. Corp.*, 895 F. Supp. 2d 1206 (N.D. Ala. 2012) (court excluded plaintiff's maxillofacial surgeon from providing expert testimony on the cause of osteonecrosis, as his education, training and experience had little to do with determining the cause of osteonecrosis.)

Moreover, the fact that Dr. Scialli read literature articles on Peters-Plus does not qualify him to diagnose Peters-Plus, as he admits that diagnosing genetic conditions is outside his area of expertise. (Scialli Dep. 24:7-26:10, Doc. 129, PageID 15156.) As explained by the court in *Mercurio v. Nissan Motor Corp.*, 81 F. Supp. 2d 859 (N.D. Ohio 2000), if an expert is not qualified in the field, the fact that such expert reviewed a significant number of articles discussing the subject only makes him "an educated lay witness who has read a few articles on the subject." *Id.* at 863. Dr. Scialli never examined or saw Plaintiff M.B.D. before opining that she has Peters-Plus. (Scialli Dep. 123:15-124:5, Doc. 129, Page ID 15181.)

2. Dr. Scialli Lacks A Reasonable Basis To Opine That The Label Is Adequate

Dr. Scialli offers no opinion on whether Depakote causes birth defects, but nonetheless opines that the label is adequate. Defendants assert that it is not necessary for their experts to have an opinion on whether Depakote causes birth defects before opining on whether the label was adequate. However, this is a failure to warn case and the main issue is whether Abbott failed to adequately warn of the risks of birth defects from Depakote. In order to answer such a question, it is essential that Defendants' experts must first have an opinion as to whether Depakote causes birth defects. Only then can they opine as to whether the label was adequate. *Reece v. Astrazeneca Pharms.*, 500 F. Supp. 2d 736, 749 (S.D. Ohio, 2007), citing *Seley v. G.D.*

Searle & Co., 423 N.E.2d 831 (Ohio 1981) (a drug label warning is adequate if it reasonably discloses all risks inherent in the use of the drug which the manufacturer knew or should have known to exist).

Furthermore, courts have excluded expert testimony as to the adequacy of a warning when there was no testimony as to causation. In *Miller v. Pfizer, Inc.*, 196 F. Supp. 2d 1062 (D. Kan. 2002), plaintiff brought a failure to warn claim against defendant after her son committed suicide following use of Zoloft. Plaintiff relied upon an expert psychiatrist and neuropsychopharmacologist to give expert testimony on general causation, specific causation and defendant's failure to warn. The court excluded the expert's testimony on general and specific causation finding that the expert's methodology was unreliable. As to the testimony on defendant's failure to warn, the court explained "[i]f the jury will hear no evidence that Zoloft causes suicide, it cannot possibly conclude the Zoloft labels do not adequately warn against the danger that Zoloft causes suicide." *Id.* at 1089. *See also, Blanchard v. Eli Lilly & Co.*, 207 F. Supp. 2d 308, 322 (D. Vt. 2002) ("without expert testimony that Prozac caused the deaths, it is not possible to show that any inadequacy in warning about Prozac was a substantial factor in bringing about the deaths."); *DeVito v. Smithkline Beecham Corp.*, No. 02-cv-0745, 2004 U.S. Dist. LEXIS 27374, *36 (N.D.N.Y., Nov. 29, 2004) (court excluded general causation expert and thereafter concluded there was no reason to analyze whether plaintiff's expert opinions on defendant's failure to warn passed muster under *Daubert*); *Rimbert v. Eli Lilly & Co.*, No. 06-0874, 2009 U.S. Dist. LEXIS 68851, *30 at fn. 12 (D.N.M., July 21, 2009) (same).

The two cases cited by Defendants do not support the proposition that courts "routinely allow experts to testify on label adequacy without proffering opinions on causation." In *Mathews v. Novartis Pharms. Corp.*, Case No. 3:12-cv-314, 2013 U.S. Dist. LEXIS 153519

(S.D. Ohio, Sept. 25, 2013), there was never any argument by either party that an expert lacked a sufficient basis for his/her opinions about the adequacy of the label for bisphosphonate drugs because he/she had no opinion about the risks associated with the drug. As such, the court did not address this issue. In *Piskura v. Taser Int'l, Inc.*, Case No. 1:10-cv-248, 2013 U.S. Dist. LEXIS 107611 (S.D. Ohio, July 31, 2013), plaintiffs alleged that defendants failed to adequately warn police about the cardiac risks of TASER shots to a person's chest. *Id.* at 3. Contrary to the case at hand, plaintiffs' warnings expert was relying upon another expert witness who would be testifying as to the medical effects of TASER shots to a person's chest. *Id.* at *29. In addition, plaintiffs' warnings expert witness had reviewed medical and scientific literature regarding the medical effects of TASER chest shots. *Id.* at *31.

Dr. Scialli's methodology, in which he purports to judge the warning adequate when he in fact has no opinion as to what the risk actually is, cannot be considered sound. Therefore, his testimony on the adequacy of the label must be excluded.

3. Dr. Scialli's Opinions Concerning Regulatory Compliance Are Contrary To Law And Must Be Excluded

Dr. Scialli offers opinions that "with respect to its FDA-approved product, valproic acid, Abbott complied with FDA requirements," and "[a]t all times prior to and during Ms. Rheinfrank's pregnancy with [M.B.D.], in addition to being consistent with applicable regulatory requirements, safety information regarding pregnancy supplied by the manufacturer (Abbott) to the FDA was adequate and appropriate." (Scialli Report, Dep. Ex. 950, Doc. 129-1, PageID 15249.) Such opinions are beyond his area of expertise, unsupported by an adequate basis, contrary to law and, therefore, must be excluded.

Plaintiffs did not mischaracterize Dr. Scialli's work history. Dr. Scialli testified that he has never been an employee of a drug company. (Scialli Dep. 167:23-168:1, Doc. 129, PageID

15192.) Although Dr. Scialli has acted as a "special government employee" for FDA, he has never been a regulatory full-time employee of FDA. (Scialli Dep. 168:11-24, Doc. 129, PageID 15192.) A "special government employee" is an officer or employee who is retained, designated, appointed, or employed to perform temporary duties, with or without compensation, for not more than 130 days during any period of 365 consecutive days. 18 USC § 202. In fact, a search of the FDA database of employees reveals that Dr. Scialli is not "an employee of FDA." (*See*, http://directory.psc.gov/employee.htm.) It is clear that Dr. Scialli is stretching his qualifications.

Contrary to Defendants' assertion, Dr. Scialli does not have knowledge of the FDA regulatory matters at issue in this litigation. Dr. Scialli testified that he doesn't know what obligations a company has in regards to adverse events, nor does he know any of the regulations governing such responsibilities (other than submission of AERs to FDA). (Scialli Dep. 149:4-22, Doc. 129, PageID 15187.) Dr. Scialli could not define the components of a pharmacovigilance plan and was unaware if any drugs had ever been removed from the market based solely on adverse events. (Scialli Dep. 148:19-151:15, Doc. 129, PageID 15187-88.) He testified that he did not know what a manufacturer's responsibility was to revise its label once it became aware of off-label use of its drug. (Scialli Dep. 227:6-10, Doc. 129, PageID 15207.) Dr. Scialli had no opinion on what a drug company should do in regard to comparing adverse event reports to historic rates, and he had no opinion to offer in regards to Abbott's data mining activities. (Scialli Dep. 153:24-154:6, 156:18-22, Doc. 129, PageID 15188-89.) As to drug company responsibilities, Dr. Scialli testified he did not know if there was a regulatory prohibition upon drug companies initiating their own safety studies. (Scialli Dep. 157:10-15, Doc. 129, PageID 15189.) (Obviously there is not.) He repeatedly denied that a manufacturer

has an obligation to assure product safety, and instead postured that the only obligation of a drug company is to report potential safety issues to FDA and then wait for instructions. (Scialli Dep. 212:3-24, Doc. 129, PageID 15203.)

Contrary to Defendants' assertion, Dr. Scialli did not unequivocally testify that the manufacturer bears responsibility for the content of its label. Dr. Scialli qualified every answer about a manufacturer's responsibility about its label with "subject to FDA approval." (Scialli Dep. 170:15-175:12, Doc. 129, PageID 15193-94.) In fact, the testimony half quoted by Defendants states: "The manufacturer bears responsibility **subject to approval by the FDA.**" (Scialli Dep. 174:13-14, Doc. 129, PageID 15193) (emphasis added.) Dr. Scialli testified: "The manufacturer and the FDA together bear responsibility for the labeling." (Scialli Dep. 173:4-7, Doc. 129, PageID 15194.) Such testimony is contrary to law and, therefore, should be excluded. *Wyeth v. Levine*, 555 U.S. 555 (2009); *In re Gadolinium-Based Contrast Agents Prods. Liab. Litig.*, MDL No. 1909, 2010 U.S. Dist. LEXIS 43444 at *109-112 (court excluded expert testimony on FDA drug approval and labeling process as it was contrary to the law in *Wyeth v. Levine*.) While Plaintiffs agree that FDA can reject a labeling change made by a manufacturer through a CBE-0, that does not change the fact that the manufacturer bears responsibility for the labeling; not the manufacturer and FDA, as Dr. Scialli testified. In fact, the court in *Wyeth* explained the CBE-0 regulation for label changes reflects "the manufacturer's ultimate responsibility for its label." *Id.* at 571.

Dr. Scialli clearly lacks the qualifications and knowledge to opine regarding compliance with FDA regulations by Abbott, and his testimony must therefore be excluded.

B. Motion To Exclude The Testimony Of Dr. Max Wiznitzer

Plaintiffs move to preclude Dr. Wiznitzer from testifying about (1) the adequacy of the

labeling; and (2) that M.B.D. does not have autism. Defendants agree that it will not offer any opinions on autism by Dr. Wiznitzer, as Plaintiffs have stated that no claim for autism or autism spectrum disorder is being pursued in this litigation. Therefore, it appears that only the opinions on labeling remain at issue. As set forth below, Dr. Wiznitzer's opinions must be excluded.

1. Dr. Wiznizter's Opinion On The Adequacy Of The Label Is Unreliable

a) Dr. Wiznitzer Has No Opinion On Causation And Failed To Review The Published Literature On Depakote Teratogenicity

As with Dr. Scialli, Dr. Wiznitzer offers an opinion as to the adequacy of the warning in the label without first having formed an opinion which he intends to offer as to whether Depakote causes birth defects. (Wiznitzer Dep. 12:8-12, Doc. 128, PageID 15011.) As set forth above, Dr. Wiznitzer's failure to opine on the causation issue renders his opinions on the adequacy of the label unreliable. Therefore, such opinions must be excluded.

Defendants argue that Dr. Wiznitzer's opinions are based on much more than three "consensus guidelines" articles, as he has "read numerous articles in the past regarding the teratogenic effects of Depakote," he is relying on "his training and education," and he has "extensive experience with, and knowledge of, Depakote's label." However, Dr. Wiznitzer only cites to three articles in his expert report: a 1992 Consensus Guideline, a 1998 Practice Parameter, and a 2002 article by Meador. (Wiznitzer Dep. Ex. 1, Doc. 128-1, PageID 15040.)

Rule 26(a)(2) is clear. It states that an expert witness must provide a written report which contains "a complete statement of all opinions the witness will express **and the basis and reasons for** them." Fed. R. Civ. P. 26. Dr. Wiznitzer's expert report cites to only 3 published sources in support of his opinions, none of which are even original articles reporting study results on Depakote. Although Dr. Wiznitzer claims to rely on articles he has read in the past, he could not recall the names or authors of any such articles. (Wiznitzer Dep. 10:19-23, 40:22-41:16,

Doc. 128, PageID 15011, 15018.) As Plaintiffs noted in their Motion to Exclude, there are scores of original articles regarding birth defects caused by Depakote. (Pls. Motion to Exclude, Ex. A, Doc. 136-1, PageID 19303.) Dr. Wiznitzer failed to consider such articles when forming his opinions in this case. Therefore, his methodology is unreliable and such opinions should be excluded.

Contrary to Defendants' assertion, Dr. Wiznitzer does not have "extensive experience with, and knowledge of, Depakote's label." Dr. Wiznitzer testified that the only Depakote labels he reviewed for his opinions were the 2003 and 2004 label. (Wiznitzer Dep. 9:12-22, Doc. 128, PageID 15010). Dr. Wiznitzer was not familiar with the warnings in the original Depakene label. (Wiznitzer Dep. 31:5-11, Doc. 128, PageID 15016.) Dr. Wiznitzer believed that the last revision to Depakote was "somewhere around 2009, 2010," even though at the time of his deposition Abbott had just revised the label four months earlier. (Wiznitzer Dep. 69:14-18, Doc. 128, PageID 15025.) Nor did Dr. Wiznitzer review the 2014 label when forming his opinions. (Wiznitzer Dep. 70:1-14, Doc. 128, PageID 15026.)

Dr. Wiznitzer's methodology is unreliable and, therefore, his opinions must be excluded.

2. Dr. Wiznitzer's Testimony About The Knowledge Of The Medical Community Is Speculative

In response to Plaintiffs' argument that, under the law, Dr. Wiznitzer is not permitted to opine on the alleged understanding of every prescribing doctor in the United States, Abbott disingenuously asserts that "Dr. Wiznitzer is not substituting his own opinion for that of the entire medical community," and he is "merely opining about what was knowable by Abbott by reference to what was then the consensus in the community of doctors." However, Dr. Wiznitzer's testimony is clear:

Q. When you talk about the warnings, clearly advised prescribing physicians,

are you talking about prescribers of antiepileptic drugs?

A. Prescribers of Depakote.

Q. And, Doctor, are you holding yourself out as representing what prescribing physicians everywhere knew about the risks of Depakote as of 1996?

A. I'm holding myself out as to what neurologists know.

Q. And that would be all neurologists in the United States as of 1996?

A. Yes. All neurologists knew or should have known.

(Wiznitzer Dep. 36:12-24, Doc. 128, PageID 15017.) This testimony is in direct contradiction to Defendants' assertion that "Wiznitzer also does not purport to speak for all neurologists." (Defs. Resp. brief, Doc. 186, PageID 24689.) Nowhere in his deposition does Dr. Wiznitzer testify about what was knowable by Abbott.[4] Nor does Dr. Wiznitzer's report discuss what was knowable by Abbott. As such, he should not be permitted to provide such opinions at trial. *R.C. Olmstead, Inc. v. CU Interface, LLC.*, 606 F. 3d 262, 270-71 (6th Cir. 2010).

The case law is clear that Dr. Wiznitzer may not opine as to the knowledge of the medical community as such testimony is speculative. *Pfizer Inc. v. Teva Pharms USA, Inc.*, 461 F. Supp. 2d 271 (D.N.J. 2006) (court held that although a physician may have 20 years of experience in the field and prescribe the drug, that does not qualify him as an expert "about what all doctors generally consider when making prescription decisions;" nor can he testify "as to all physicians' understanding of the risks and benefits" of the drug.); *Bartlett v. Mut. Pharm. Co.*, 742 F. Supp. 2d 182, 195 (D.N.H. 2010) (court precluded expert from testifying about what doctors generally know as such testimony is speculative); *In re Baycol Prods. Litig.*, 532 F. Supp. 2d 1029, 1069 (D. Mn. 2007) (court held that expert physician could not provide expert testimony "as to what other physicians knew or would have done with different information."); *In re Rezulin Prods.*

[4] If Dr. Wiznitzer's opinions were not clear based on his testimony, Abbott's counsel had the opportunity to clarify his testimony during the deposition, yet no questions were asked of Dr. Wiznitzer by Abbott's counsel.

Liab. Litig., 309 F. Supp. 2d 531 (S.D.N.Y. 2004) (court excluded expert testimony regarding physicians' practices of reading drug labels and the understanding of such labels as such testimony was speculative.)

Moreover, Plaintiff Rheinfrank's Depakote prescription in 2003 was not prescribed by a neurologist, but rather an internal medicine resident at an outpatient clinic at Good Samaritan Hospital. Therefore, even if he could somehow speak for all neurologists, that testimony would be irrelevant to the facts of this case. Expert testimony which fails to "fit" the case is also excludable under *Daubert. Pride v. BIC Corp.*, 218 F.3d 566, 578 (6th Cir. 2000).

Abbott tries to assert that Dr. Wiznitzer was opining about what was knowable by Abbott by reference to "what was the consensus in the community of doctors who had the most experience with AEDs." However, that was not his testimony, nor was that stated in his report. Instead, a review of the consensus guidelines cited by Dr. Wiznitzer reflects the thinking by certain members of the medical community concerning data on AEDs. However, it is not up to the medical community to figure out if Depakote is more teratogenic than other AEDs; it's Abbott's job as the manufacturer to do the research on its drug and advise the medical community of all the risks of Depakote. *See Proctor v. Davis*, 291 Ill. App. 3d 265, 278 (Ill. App. Ct. 1st Dis. 1997) (the drug manufacturer could not fulfill its duty "merely by waiting for what it considered sufficient proof of a cause-effect relationship before advising the medical profession with an appropriate alert or warning of the possibility of risk in the use of one of its products.") In fact, each of the three articles cited by Dr. Wiznitzer discusses the need for research to help determine the relative safety of these drugs. Nowhere in his report does Dr. Wiznitzer discuss what Abbott could have known as a manufacturer, what research it could have done, or what information it actually internally had that had not been published. Defendants

cannot recast their expert testimony and reports to pretend that the expert offered an opinion that he never gave.

Furthermore, even if, as Defendants' suggest, Dr. Wiznitzer is opining as to what was knowable by Abbott, such opinions would lack a reasonable basis. Dr. Wiznitzer can hardly give an opinion as what was knowable by Abbott when the only articles he reviewed to support his opinions were the three non-original articles cited in his report. Dr. Wiznitzer did not conduct his own literature search to determine what was knowable by Abbott on birth defects caused by Depakote. (Wiznitzer Dep. 46:21-47:9, Doc. 128, PageID 15020.) Nor did Dr. Wiznitzer review any internal Abbott documents or testimony by Abbott employees in rendering his opinions. (Wiznitzer Dep. 11:5-23, Doc. 128, PageID 15011.) Any such supposed opinions by Dr. Wiznitzer lack a reliable basis.

C. Motion To Exclude The Testimony Of Dr. Stephanie Greene

1. Dr. Green Is Unqualified To Opine On The Cause Of M.B.D.'S Chiari I Malformation

Dr. Greene opines that Depakote does not cause Chiari I malformation nor did it cause M.B.D.'s specifically. Simply, as a neurosurgeon, Dr. Greene does not have the requisite education, training, or experience to determine the cause of Chiari I malformation. Fed. R. Evid. 702. Defendants reiterate Dr. Greene's extensive credentials as a surgeon, none of which qualify her to opine on etiology. As Plaintiffs have previously acknowledged, Plaintiffs do not doubt that Dr. Greene is an accomplished neurosurgeon. Nor do Plaintiffs dispute Dr. Greene's conclusions that M.B.D. suffers from Chiari I malformation, that M.B.D.'s surgery was necessary, and that the surgery was effective, as these are within her ken of expertise. (Greene Dep. 21:1-5, Doc. 127, PageID 14941; Green Report, Dep. Ex. 2, Doc. 127-1, PageID 14959 at 14963.)

Defendants counter that Dr. Greene treats patients with Chiari I and has "regularly diagnosed craniosynotosis, which is commonly associated with Chiari I." These facts, however, have no bearing on the determination of etiology for Chiari I malformation. In contrast to the surgical field, etiology is the study of what caused the diagnosed disorder, not merely what the diagnosis is. *Tamraz v. Lincoln Elec*. Co., 620 F.3d 665, 673 (6th Cir. Ohio 2010). The Sixth Circuit has firmly distinguished etiology from diagnosis and characterized the two medical functions as "not remotely the same…" *Gass v. Marriott Hotel Servs*., 558 F.3d 419, 426 (6th Cir. 2009) (citations omitted). To that end, most treating physicians have more training and experience with diagnosis than etiology. *Tamraz*, 620 F.3d at 673.

Such is the case for Dr. Greene, as Defendants are unable to point to any experiences Dr. Greene has where she had to identify the cause, not merely diagnose or treat, a Chiari I malformation. This is unsurprising considering that she does not so much as understand the mechanism by which Depakote causes birth defects. (Greene Dep. 42:9-12, Doc. 127, PageID 14947.) Defendants leave uncontested her testimony that "to determine the extent of the effect valproic acid had on [M.B.D.] and her development," she would defer to a dysmporphologist or a genetics teratologist. (Greene Dep. 51:3-10, Doc.127, PageID14949.) Further, even the case Defendants cite weighs in favor of excluding her: "simply because a doctor has a medical degree does not make [that doctor] qualified to opine on all medical subjects." *Gayton v. McCoy*, 593 F.3d 610, 617 (7th Cir. 2010).

Dr. Greene's lack of expertise in this field is further underscored by her deposition testimony that she is not sure that M.B.D.'s Chiari I malformation is related to her exposure to Depakote. (Greene Dep. 51:3-10, Doc.127, PageID 14949.) In contradistinction to Plaintiffs' competing expert, Dr. Greene cannot identify the cause for M.B.D.'s Chiari I malformation.

(Green Report, Dep. Ex. 2, Doc. 127-1, PageID 14963.) Thus, although Dr. Greene is a medical doctor and is qualified to opine on the diagnosis and treatment of Chiari I malformation, which she has done, her opinion regarding the etiology of M.B.D.'s Chiari I malformation is beyond her ken of expertise and should be excluded under Rule 702.

2. Dr. Greene's Testimony Is Unreliable Because She Failed To Rely Upon Valid, Scientific Methodology

Defendants' claim that "Dr. Greene's opinions are based on her substantial clinical experience and an exhaustive review of published literature" is not compelling. First, Dr. Greene's "review of published literature" was clearly not exhaustive. In drafting her report, Dr. Greene was unaware of three other cases where a mother's Depakote use during pregnancy was associated with Chiari I malformation in her child. (Greene Dep. 36:18-38:6, Doc.127, PageID 14945-46.) Two of these reports were articles in the published medical literature. (Williams, et al., Yeboa Dep. Ex. 931, Doc. 81-1, Page ID 2525-29; LaJeunie, et al., Yeboa Dep. Ex. 932, Doc. 81-1, PageID 2535-39.) Defendants attempt to minimize the significance of missing a "few" cases, but only one in 1000 people who have undergone diagnostic brain imaging have a Chiari I malformation, so ignoring three reported cases was a critical error on Dr. Greene's part. (Yeboa Dep. Ex. 938, Doc. 81-2, Page ID 2624.) This oversight demonstrates that Dr. Greene's search was not in any way comprehensive. (Green Report, Dep. Ex. 2, Doc. 127-1, PageID 14963.) Even with the limited information she did have, Dr. Greene admits that she never attempted to conduct any analysis on the data. (Greene Dep. 40:20-24, Doc.127, PageID 14946.) Such a methodological shortcoming diminishes the reliability of Dr. Greene's opinion.

Furthermore, Defendants' remaining support for Dr. Greene's methodology, that she has "substantial clinical experience," carries little weight. Plaintiffs do not contest that Dr. Greene has seen thousands of Chiari patients as she claims. The problem lies in the fact that, out of all

those thousands of cases she had, she did not review the records of a single one before testifying. Dr. Greene claimed to rely upon her personal experience as to whether her patients had been exposed to Depakote in utero, yet she failed to actually conduct any type of internal review of her own patients' files to identify cases of Chiari I malformation associated with Depakote exposure. (Greene Dep. 13:15-20, Doc.127, PageID 14939.) It is nigh impossible that, of the 6,000 Chiari I patients Dr. Greene claims she has seen, she is able to accurately recollect, from memory alone, the details of which teratogens her patients were exposed to. Furthermore, due to her lack of review of these records, whatever data exists about her patients and whether they had been exposed to Depakote is unavailable. She provides no data to support her opinion. Rather, it's just her unconfirmed impression with no data to confirm or deny her statement.

Ultimately, Defendants are unable to meet their burden to show by a "preponderance of proof" that Dr. Greene meets the *Daubert* admissibility standards to opine upon the cause of M.B.D.'s Chiari I malformation. *See Pride v. BIC Corp*., 218 F.3d 566, 578 (6th Cir. 2000). Dr. Greene's opinion lacks the "intellectual rigor" required for expert testimony to be admitted under Federal Rule of Evidence 702 and *Daubert*. *See Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152 (1999). None of her opinions are capable of replication, have been subject to peer review, or otherwise satisfy the strictures set forth in *Daubert*. Her practical experience and academic background, even when taken into account, do not qualify her opinion in this area. *Kumho* 526 U.S. at 152.

II. CONCLUSION

For the foregoing reasons, Plaintiffs respectfully request that this Honorable Court grant their motion to exclude the opinions and anticipated testimony of Abbott's experts, Dr. Kwame Anyane-Yeboa, Dr. Anthony Scialli, Dr. Max Wiznitzer, and Dr. Stephanie Greene.

Respectfully submitted,

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Certificate of Service

I hereby certify that on the 30th day of March, 2015 a copy of the foregoing was filed electronically with the Clerk of the Court, to be served via the Court's electronic filing system on all counsel of record, and was also submitted in hard copy form to this Court's chambers.

/s/ *Janet G. Abaray*
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